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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,445	03/03/2005	Wangxia Wang	29374	9670

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,445	WANG ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *132-146,148-154,171 and 172* is/are pending in the application.

4a) Of the above claim(s) *138-143,146,148-154,171 and 172* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *132-137,144 and 145* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01.19.09; 01.28.09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election of the species, protein of an agent of a non-infectious disease, in the reply filed on January 14, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Regarding paragraph 1, page 2 of the December 17, 2008 Office action, the lines directed to an inhibitor of angiogenesis, were inadvertently included in that Office action. The lines should have read: Upon review of Applicants' amendments, it appears that a restriction requirement is necessary because each of the polypeptide molecules are structurally and functionally distinct.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 1-131, 147, 155-170, 173-176 are canceled. Claims 138-143, 146, 148-154, 171-172 are withdrawn. Claims 132-137, 144-145, to a protein of an agent of an infectious disease, are currently under examination.

Priority: The benefit date of September 2, 2002, is acknowledged.

It is also noted that the IDS submitted January 28, 2009 appears to be a duplicate of the IDS submitted February 8, 2009; therefore only the IDS of January 28, 2009 has been considered.

Objections and Rejections

Claim 132 is objected to because of the following informalities: claim 132 recites "a boiling stable polypeptide" and then recites "said boiling stable protein." It is unclear if "said boiling stable protein" is the same as the "boiling stable polypeptide". Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 132-135, 144-145 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein comprising SEQ ID NO: 2 fused to an additional polypeptide to have stability against boiling, does not reasonably provide enablement for fusion proteins comprising variants of SEQ ID NO: 2 fused to the additional polypeptides listed in claim 132, to have stability against boiling. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which fusion proteins comprising variants of instant SEQ ID NO: 2 and an additional polypeptide will function in the same way as the wild-type protein depicted as SEQ ID NO: 2, as well as maintain the activity of the additional polypeptide. Thus there could be thousands of variants of SEQ ID NO: 2 which contain

substitutions, deletions, additions etc. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which fusion proteins were active.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are myriad combinations to choose from, i.e. variants of SEQ ID NO: 2 fused to a protein of an agent of an infectious disease. The amount of guidance in the specification is minimal with regard to which amino acids in instant SEQ ID NO: 2 are essential for activity. No working examples are present of variants of instant SEQ ID NO: 2 fused to an additional polypeptide. The nature of the

invention is such that many different proteins that are substantially similar to instant SEQ ID NO: 2 may or may not be boiling stable. The state of the prior art is that even proteins that are 99% similar to the wild-type protein are at times not fully active. The relative level of skill in this art is very high.

The predictability as to what substantially similar protein will have which activity is zero. When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

In their remarks received February 28, 2008, Applicants submit Tables I and II, which summarize the sequence and structural similarity between boiling and detergent-stable proteins from Aspen (SEQ ID NO: 2) and other, diverse plant species (Tomato, Pine, Rice, Corn, and Arabidopsis) having at least 65% amino acid homology to SEQ ID NO: 2. Applicants' arguments have been fully considered but they are not persuasive.

The instant claims have been amended and are now directed to fusion proteins comprising a boiling stable protein having at least 65% identity to SEQ ID NO: 2 fused to an additional polypeptide, i.e. a protein of an agent of an infectious disease. As noted above, the specification only appears to be enabled for a fusion protein comprising SEQ ID NO: 2 fused to an additional polypeptide. Therefore, the instant specification does not reasonably provide enablement for fusion proteins comprising variants of SEQ ID NO: 2 fused to an additional polypeptide, having stability against boiling.

Claims 132-135, 144-145 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to fusion proteins comprising a boiling stable protein having at least 65% identity to SEQ ID NO: 2 fused to a protein of an agent of an infectious disease, to have stability against boiling. *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As stated above, the claims are directed fusion proteins comprising a boiling stable protein having at least 65% identity to SEQ ID NO: 2 fused to a protein of an agent of an infectious disease, to have stability against boiling. However, the skilled artisan cannot necessarily envision the detailed structures of ALL of the variants of the polypeptide depicted as instant SEQ ID NO: 2 that have the same functional activity as the wild-type polypeptide of instant SEQ ID NO: 2 fused to a protein of an agent of an infectious disease because nowhere in the specification is it described which amino acids are even essential and critical for the wild-type protein to maintain its functionality, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the

invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Applicants have amended claims 132-137, 144-145.

The claims are rejected under 35 U.S.C. 112, first paragraph, written description, because it appears that Applicants only have possession of a fusion protein comprising SEQ ID NO: 2 fused to an additional polypeptide and not all the variants of SEQ ID NO: 2 fused to said additional polypeptide.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 144-145 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 145, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 144-145 recite the limitation "said protein of non-infectious diseases" in the claims. There is insufficient antecedent basis for this limitation in the claims and their parent claims. The parent claim 132 recites "a protein of an agent of an infectious disease."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 132-137, 144-145 are rejected under 35 U.S.C. 102(e) as being anticipated by Wang et al. (US 20050074763; IDS).

The applied reference has five common inventors with the instant application. The Oath/Declaration lists eight inventors for the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Wang et al. teach SP1, a boiling stable, detergent stable, and protease resistant protein having chaperone-like activity that is purified from aspen plants (p. 8 [0100]). Wang et al. also teach SEQ ID NO: 2 (which has 100% sequence identity to instant SEQ ID NO: 2) that describe a boiling stable, detergent stable, and protease resistant protein having chaperone-like activity, is natively an oligomer, and able to heat stabilize proteins (p. 27-28 pgpub claims 46, 56, 66). Wang et al. further teach a fusion protein comprising boiling stable, detergent stable, and protease resistant protein having chaperone-like activity (p. 29 claim 84; claims 132-137, 144-145), where the additional polypeptide can be proteins from non-infectious diseases, such as

poorly antigenic autologous tumor cell proteins or any of their epitopes (p. 17 [0192]; claims 132-137, 144-145).

In their remarks received February 28, 2008, Applicants assert the instant specification includes all of the disclosures of both PCT IL03/0023 and PCT IL02/00174, and as such includes the entire disclosure of Wang et al. (US 20050074763). A petition for unintentional delayed claim of priority, according to 37 U.S.C. 1.78(a)(3) is being filed, along with requisite fees, effectively determining identical priority for the present application and the cited publication. Applicant's arguments have been fully considered but they are not persuasive.

Applicants' petition to accept an unintentionally delayed claim of benefit of earlier filing date and cross reference to other applications (37 CFR 1.78(a)(6)) filed February 28, 2008, has been dismissed without prejudice (decision on December 3, 2008). Therefore, the priority date of the instant application is acknowledged as September 2, 2002; and therefore, Wang et al. (US 20050074763) is believed to be relevant art under 35 U.S.C. 102(e).

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/
Primary Examiner, Art Unit 1656

April 1, 2009